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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/678,357	10/04/2000	Sven Mardh	SMAR.P001	4507

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EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/26/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/678,357	MARDH ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 6/04/2002, paper # 8 has been entered.

Applicants' Amendments

2. Acknowledgement is made of Applicants' amendments filed 6/04/2002 paper number 9, which have been entered.

Status of the Claims

3. Claims 4 and 6-13 have been canceled; new claims 14-43 have been added.

Claims 14-43 are pending and under consideration.

Prior Citations of Title 35 Sections

4. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Rejection (s) Moot

5. The rejection of claims 4, 6, and 7 made on pages 3 and 4 of the office action mailed 12/21/2001 (paper no. 7) under 35 U.S.C. 112 first paragraph is moot in light of applicants' cancellation of the claims.

Rejection (s) Maintained

6. The rejection of claims 4, 6-8 made on pages 4 and 5 of the office action mailed

12/21/2001 (paper no. 7) under 35 U.S.C. 102 (b) is moot in light of applicants' cancellation of the claims, however the rejection is maintained in view of the new claims 14-38 because the new claims are drawn to the same invention as cancelled claims.

The rejection is as stated below:

Claims 14-38 are rejected under 35 U.S.C. 102 (b) as being anticipated by Lindgren et al. (European Journal of Gastroentrology and Hepatology, Volume 10, Number 7, pp 583-588, July 1998).

Claims 14-38 are drawn to a method of diagnosing gastritis by evaluating blood samples for the presence of antibodies for H, K-ATPase, *Helicobacter pylori* and the concentration of pepsinogen I by immunoassay.

Lindgren et al. teach a method of diagnosing gastritis comprising evaluating blood samples for the presence of antibodies for H, K-ATPase, *Helicobacter pylori* and the concentration of pepsinogen I by immunoassay (see abstract).
They further teach a method to compare the diagnostic performance of serum antibodies to H, K-ATPase, serum Pepsinogen A (same as Pepsinogen I) and the Schilling test in diagnosing chronic atrophic body gastritis; to study the interrelationships between H, K-ATPase antibodies, serology for *Helicobacter pylori*, and gastric morphology. Lindgren et al. teach relationship of the values of indicators in relation to different gastric pathologies (See table 1., page 585).

Applicants' arguments filed 06/04/2002 have been fully considered and are not persuasive. Applicants argue, " As was previously noted, the Lindgren article performs the same tests as

called for in the present method, but wholly lacking in any indication that the result of the tests can be used in combination."

It is the examiner's position that claims are drawn to a method for screening for gastritis by evaluating three indicators H,K-ATPase , *Helicobacter pylori* antibodies and the concentration of pepsinogen by immunoassay. It would appear even by applicants own admission (as recited above) that Lindgren article meets the limations recited in the claims. Applicants state that Lindgren's article " performs the same tests as called for in the present invention" Since the methods appear to be the same as the claimed method, then inherently one would also use the results of the tests in combination to classify the conditions. Lingren et al teaches not only the diagnostic performance of each test but also compare the various indicators in combination to classify the conditions (see morphological and serological findings and table 1 in page 585). Applicants further argue that Lindgren reference does not teach each and every element of the newly submitted method claim 14. The Examiner respectfully disagree for the reasons stated above and Lindgren reference anticipates the newly submitted claim 14. As in regard to the new added limitaions in claims 19 and 20 about the autoimmune aspect of gastritis. Lindgren et al. recite the relation of H,K-ATPase and autoimmnue gastric atrophy (see Lindgren reference pages 583 and 587).

7. The rejections of claims 9-13 made on pages 5, 6 and 7 of the office action mailed 12/21/2001 (paper no. 7) under 35 U.S.C. 103(a) are moot in light of applicants' cancellation of the claims, however the rejection is maintained in view of the new claims 39-43 because the new claims are drawn to the same invention as cancelled claims.

Claims 39-43 are rejected under U.S.C. 103 (a) as being unpatentable over Lindgren et al

Claims 39-43 are drawn to a kit for screening method for gastritis comprising reagents suitable for detecting H, K- ATPase antibodies, *Helicobacter pylori* antibodies, and Pepsinogen I.

Lindgren et al. teach a screening method for gastritis, evaluting blood samples for the presence of antibodies for H, K-ATPase , Helicobacter pylori and the concentration of pepsinogen A (pepsinogen I) . They also disclose that the antibodies to H, K-ATPase were determined using an enzyme- linked immunoabsorbent assay, Helicobacter pylori antibodies were determined using enzyme immunoassy, and pepsinogen I serum level was determined by a double - antibody radioimmunoassy. Lingren et al. did not teach a kit comprising the above reagents.

At the time the invention was made, it would have been prima facie obvious to a person of ordinary skill in the art to combine the reagents and methods taught by Lindgren et al. in form of a kit for screening gastritis.

Applicants' arguments filed 06/04/2002 have been fully considered and are not persuasive.

Applicants argue that " allegedly obvious must be assembled for some purpose, or there would be no motivation to make a kit".

It is the examiner's position that Lindgren et al. teach the reagents and the method as claimed by the applicants. At the time the invention was made, it would have been *prima facie* obvious to a person of ordinary skill in the art to combine the reagents and methods taught by Lindgren et al. in form of a kit for screening gastritis and one of ordinary skill in the art would have been motivated to assemble the reagents of well-known and obvious tests in form of a kit for mere convenience and to simplify and optimize diagnostic techniques to detect multiple antibodies in the same sample. Supplying three immunoassay indicators in form of a kit comprising reagents suitable for the above well-known indicators, and including an immobilized solid support, labeled antibodies, and buffers are well known in the art. Assembling the reagents of well-known and obvious tests in form of a kit is for mere convenience and does not impart any criticality on the patentability of a well-known test or procedure.

8. The rejections of claims 9-13 made on pages 5,6 and 7 of the office action mailed 12/21/2001 (paper no. 7) under 35 U.S.C. 103(a) are moot in light of applicants' cancellation of the claims, however the rejection is maintained in view of the new claims 14-43 because the new claims are drawn to the same invention as cancelled claims.

The rejection is a stated below:

Claims 14-43 are rejected under U.S.C. 103 (a) as being unpatentable over

Oksanen et al. (Scandinavian Journal of Gastroentrology, Vol. 35, No. 8 pp 791-795, August 2000), in view of Ma J.Y. et al. (Scandinavian Journal of Gastroentrology, Vol. 29, No.11, pp961-965, 1994). Prior art already made of record.

Claims 14-43 are drawn to a method and a kit for screening gastritis assaying blood samples for the presence of H, K- ATPase antibodies, *Helicobacter pylori* antibodies, and Pepsinogen I.

Oksanen et al. evaluated serum samples to predict normal gastric mucosa by studying the serum samples for *Helicobacter pylori* antibodies by enzyme immunoassay (Pyloriset EIA-G and EIA-A) and pepsinogen I was measured by an immunoenzymometric assay (Gastrotest PGI). Oksanen et al. did not teach assaying for H, K-ATPase antibodies.

Ma J.Y. et al. studied sera from patients with pernicious anemia by means of enzyme-linked immunosorbent assay for the occurrence of antibodies against H, K-ATPase and *Helicobacter pylori.* Ma J.Y. et al. do not teach Elisa to measure pepsinogen I levels.

Limitations such as higher or lower level of the indicators or calculating ratios of the indicators are being viewed as limitations of optimizing experimental parameters.

At the time the invention was made, it would have been prima *facie* obvious to a person of ordinary skill in the art to combine the two antibody assay methods and kits taught by Oksenen et al with the method taught by Ma J.Y. et al in form a kit for

screening gastritis. The analysis of multiple analytes or more indicators associated with gastritis provides reliable method for diagnosing gastritis.

One of ordinary skill in art would have been motivated to do this in order to obtain a method and a kit to simplify and optimize diagnostic techniques to detect multiple antibodies in the same sample.

Applicants' arguments filed 06/04/2002 have been fully considered and are not persuasive.

Applicants argue that these references each teach tests for two of the three indicators specified in claim 4. Neither test, however, discloses anything about using the test results in combination.

It is the examiner's position that the applicants appear to argue that the references individually without clearly addressing the combination of references. It must be remembered that the references are relied upon in combination and are not meant to be considered separately in a vacuum. It is the combination of all the cited and relied upon references, which make up the state of the art with regard to the claimed invention. Applicants claimed invention fails to patentably distinguish over the state of art represented by the cited references. *In re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968); In *re Keller* 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

With respect to kit claims, Applicants argue that " there is no obvious reason why a person skilled in the art would be motivated to assemble the reagent into a kit".

It is the examiner's position that the combination of the references teaches the reagents, the method and the kit as claimed by the applicants. At the time the

invention was made, it would have been prima *facie* obvious to a person of ordinary skill in the art to combine the two antibody assay methods and kits taught by Oksenen et al with the method taught by Ma J.Y. et al in form a kit for screening gastritis. One of ordinary skill in art would have been motivated to do this in order to obtain a method and a kit to simplify and optimize diagnostic techniques to detect multiple antibodies in the same sample. As in regard to the new added limitaions about the autoimmune aspect of gastritis see Ma reference pages 962 and 965.

Drawings
Objections Maintained

9. The objection to the drawings in paragraph 4 of the office action mailed March 23, 2001 (paper number 4) is maintained no amendment to drawings were submitted.

New Ground for Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 19, 20, 21, 26, 27, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims now include the newly added limitations " autoimmune" and " autoimmunity". However, there appears to be no descriptive support in the instant specification

for these added limitations. Therefore the new limitation in the claim is considered new matter. *In re Rasussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step or a compound from a disclosure. See MPEP 608.04 and MPEP 2163.06.

Applicants are respectfully requested to point out the proper descriptive support in specific part (s) of the disclosure as filed, for the newly added limitations, or to remove the new matter from the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 14-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 rejected as being indefinite for reciting improper Markush group. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being " selected from the group comprising of A, B, and/or C." See exparte Markush, 1925 C.d. 126 (Comm'r Pat. 1925). It is not clear what is the scope of claim 4. It is not clear what is being detected one indicator or all of those indicator?

Claim 14 recites the phrase "diagnosing possible presence of gastritis in a human". It is not clear what applicants intend in recitation of the above phrase.

Claim 14 recites the phrase "wherein altered levels in the sample is indicative of gastritis". It is not clear what applicants intend in recitation of the above phrase. What are the altered levels?

Claim 15 recites the limitation "said indicators". There is insufficient antecedent basis for this limitation in the claim.

Claims 14, 18, 22, 25, 26, 29, 33, 34, 37, 38 and 43 recite the limitations "concentration of pepsinogen I or pepsinogen I concentration". It is not clear what applicants intend in recitation of the above limitations.

Claim 16 is rejected under the second paragraph of 35 U.S.C. 112 as being an improper dependent claim. Claim 16 broadens the scope of claim 14, from which it depends (claim 16 depends from 15, which depends from claim 14).

Claim 14 is drawn to a Markush group consisting of 3 indicators. Claim 16 recites " The method of claim 15, further comprising the step of determing an additional indicator comprising the level of pepsinogen I multiplied by the level of *Helicobacter pylori* antibodies, and wherein the level of this additional indicator is compared to a standard." thus improperly broadens the scope of claim 14.

Claim 31 is rejected under the second paragraph of 35 U.S.C. 112 as being an improper dependent claim. Claim 31 broadens the scope of claim 14, from which it depends. Claim 14 is drawn to a Markush group consisting of 3 indicators. Claim 31 recites " The method of claim 14, further comprising the step of determing an additional indicator comprising the level of pepsinogen I multiplied by the level of *Helicobacter pylori* antibodies, and wherein the level of this additional indicator is

compared to a standard." thus improperly broadens the scope of claim 14.

The term "optionally" in claims 19, 26 and 34 is a relative term, which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 39 recites the phrase "reagents suitable for detecting antibodies". It is not clear what applicants intend in recitation of the above phrase. What reagents suitable for detecting antibodies?

Claim Rejections - 35 USC § 103

12. Claims 39-43 are rejected under U.S.C. 103 (a) as being unpatentable over Lindgren et al. in view of Harkonen, M. (WO 96/15456).

Claims 39-43 are drawn to a kit for screening for gastritis comprising reagents suitable for detecting H, K- ATPase antibodies, *Helicobacter pylori* antibodies, and Pepsinogen I.

Lindgren et al. teach a screening method for gastritis, evaluating blood samples for the presence of antibodies for H, K-ATPase, *Helicobacter pylori* and the concentration of pepsinogen A (pepsinogen I). They also disclose that the antibodies to H, K-ATPase were determined using an enzyme- linked immunoabsorbent assay, *Helicobacter pylori* antibodies were determined using enzyme immunoassy, and pepsinogen I serum level was determined by a double -antibody radioimmunoassy. Lingren et al. did not teach a kit comprising the above reagents. However, Harkonen

teaches a kit for determination of serum pepsinogen I, *Helicobacter pylori* antibodies and gastrin (see claim 12 and page 10).

It would have been prima *facie* obvious to a person of ordinary skill in the art, at the time the invention was made to combine the reagents and methods taught by Lindgren et al. and Harkonen and replace the gastrin antibody with antibodies to H, K-ATPase in the kit to obtain the instant invention. One of ordinary skill in art would have been motivated to do this in order to make a kit to simplfy and optimize diagnostic techniques to detect multiple indicators in the same sample.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from 7:30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

August 22, 2002

NITA MANNFIELD
PRIMARY EXAMINER
8/22/02